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10/534,544	05/10/2005	Shmuel Pietrokovski	29489	7801

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EXAMINER	
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ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,544	PIETROKOVSKI ET AL.	
	Examiner	Art Unit	
	OLUWATOSIN OGUNBIYI	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-121* is/are pending in the application.

4a) Of the above claim(s) *19-121* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *Claims 1-18* is/are rejected.

7)☒ Claim(s) *1-6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/26/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-121 are pending in the application. Claims 1-18 drawn to SEQ ID NO: 31 are under examination.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

The drawings in this application have been accepted. No further action by Applicant is required.

Information Disclosure Statement

The information disclosure statement filed 1/26/07 has been considered. An initialed copy is enclosed.

Election/Restrictions

Applicant's election of invention 3 (claims 1-18) drawn to SEQ ID NO: 31 in reply to the restriction requirement mailed 1/14/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

As stated in the restriction requirement on p. 3, invention 3 is drawn to a chimeric polypeptide. Invention 3 comprises the groups of invention i.e. groups 101-198, each group of an invention being drawn to a different sequence selected from SEQ ID NO: 9-106 respectively.

Claims 19-121 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions there being no allowable generic or linking claim.

Claim Objections

Claim 1 is objected to as containing non-elected species. Claim 1 contains non-elected species, which are withdrawn due to the lack of a generic claim. See election of specie – in the restriction requirement mailed 1/14/08.

Claims 2-4 and 6 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 2 is drawn to a chimeric polypeptide comprising an auto-processing segment having an amino acid sequence set forth by SEQ ID NO: 31 wherein said auto-processing segment is BIL4_cloth. The recitation of BIL4_cloth in claim 2 does not further limit SEQ ID NO: 31 of claim 1 because as written it appears that SEQ ID NO: 31 and BIL4_cloth are the same auto-processing segment. Thus, renaming SEQ ID NO: 31 as BIL4_cloth in claim 2 does not further limit the polypeptide of claim 1. As to the acronym "BIL4_cloth, acronyms are permissible shorthand in the claims but the first recitation in the claims should include the full meaning of the acronym. As to claims 3 and 4 the recitation of "said autoprocessing segment is

derived from Clostridium" (claim 3) or "Clostridium thermocellum" (claim 4) does not further limit, structurally, the polypeptide of claim 1. These are process limitations which do not further limit the instant product i.e. the polypeptide.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a chimeric polypeptide comprising an autoprocessing segment placed between two polypeptide segments wherein said autoprocessing segment comprises the amino acid sequence set forth in SEQ ID NO: 31 wherein the amino terminal of the polypeptide segment adjacent to the carboxy terminus of said autoprocessing segment has an amino acid residue comprising a nucleophilic group such as sulfhydryl or hydroxyl group and wherein said autocleavage of said chimeric polypeptide results in C-terminal cleavage , does not reasonably provide enablement for said chimeric polypeptide comprising an autoprocessing segment

between two polypeptide segments wherein said autocleavage of said chimeric polypeptide results in N-terminal cleavage or a chimeric polypeptide comprising an autoprocessing segment located at the N or C terminus end of said chimeric polypeptide.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to a chimeric polypeptide comprising an autoprocessing segment having an amino acid sequence set forth by SEQ ID NO: 31.

The specification teaches that when the protein with the amino acid sequence set forth in SEQ ID NO: 31 (aka BIL4_CLOTH) is inserted in between two protein segments autosplicing as well as carboxy terminal autocleaving occurs. Specification p. 56-57. The specification teaches that when BIL4 SEQ ID NO: 31 is placed as follows between maltose binding protein (MBP) and chitin binding domain (CBD): MBP-BIL4-CBD, the following products are obtained: MBP-CBD (MC) and MBP-BIL4 (MB). See figure 12 and the specification p. 16 under fig. 12a-c.

The specification does not teach that the fragment BC is obtained. The specification specifically concludes that cleavage occurs at the carboxy terminus of SEQ ID NO: 31 (specification p. 57 lines 5-9). There is no evidence for cleavage occurring at the N-terminus of SEQ ID NO: 31 in fig. 12. Thus, SEQ ID NO: 31 is able to carry out its auto cleavage activity at its C- terminus end when placed between to proteins (e.g. MB product) and said autocleavage results in autosplicing of the flanking polypeptides (e.g. MC product).

Claim 1 is broadly drawn to any placement of the autoprocessing segment within the chimeric polypeptide. As set forth above and in the specification, SEQ ID NO: 31 has to be

placed between to proteins so that C-terminal cleavage reaction can occur followed by the splicing reaction. The specification does not provide guidance as to whether SEQ ID NO:31 can be placed at the end, for example, BIL4-MBP-CBD or MBP-CBD-BIL4 and result in autocleavage activity. The specification teaches that certain amino acid residues have to be present adjacent to conserved amino acid residues at the C-terminal end of the autoprocessing segment (p. 3 line 15-29 and p. 20 lines 23-32 and p. 21 lines 1-23). The specification teaches that the amino terminal of the polypeptide adjacent to the carboxy terminus of the autoprocessing segment has a cysteine, serine or threonine i.e. amino acid residues comprising a nucleophilic group such as sulfhydryl or hydroxyl group for autoprocessing to occur.

As claimed the instant chimeric polypeptide has autoprocessing activity and thus for autoprocessing to occur the nucleophilic group has to be placed as set forth supra. The instant claims (except for claims 7-9) do not specify that the chimeric polypeptide comprises the nucleophilic group as set forth above necessary for autoprocessing.

As to claims 16 and 18, what is the affinity tag that is capable of binding a virus and a cell? The specification does not provide guidance as to affinity tags that bind viruses and cells as substrates. The specification teaches tags derived from viruses (bottom of p. 22) but does not teach affinity tags that bind viruses and cells. The art does not teach affinity tags that specifically binds viruses and cells. See Jarvik et al Anu. Rev. Genet. 1998, 32:601-18 for tags derived from viruses and human cells (p. 604 table 1).

Thus, in view of the teachings of the specification, the specification has taught one of skill in the art how to use the instant chimeric polypeptide comprising the instant autoprocessing

segment (SEQ ID NO: 31) for autosplicing and C-terminal autocleavage but has not taught how to use the instant chimeric polypeptide for N-terminal autocleavage.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite "chimeric polypeptide" but the metes and bounds of the content and arrangement of said chimeric polypeptide is not clear as claimed. Based on the teachings in the specification concerning SEQ ID NO: 31 (aka BIL_4 CLOTH), the autoprocessing segment is placed in between 2 proteins for autoprocessing to occur. However this arrangement is not reflected in independent claim 1. The recitation of "…said auto-cleavage results in removal of a segment of the polypeptide adjacent to an amino terminal end or a carboxy terminal end" in claim 5, lacks antecedent basis, because claim 1 from which claim 5 depends does not clearly depict how the chimeric polypeptide is arranged so that auto-cleavage can occur or autosplicing (see claim 11).

Also to the recitation of "…said auto cleavage..." in claims 5,11 and 13, this lacks antecedent basis in claim 1 because claim 1 does not mention "autocleavage" but "autoprocessing".

As to claim 13, the recitation of "capable of" makes the claim unclear because can the chimeric polypeptide perform the recited function or not under the conditions? "Capable of" is not a definite phrase.

As to claims 16 and 18, what are the affinity tags that are capable of specifically binding viruses or cells?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-12 and 15-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Chong et al The Journal of Biological Chemistry vol. 271:22159-22168, 1996 (IDS).

The claims are drawn to a chimeric polypeptide comprising an autoprocessing segment having an amino acid sequence set forth by SEQ ID NO: 31.

Chong et al teach a chimeric polypeptide comprising an autoprocessing segment having an amino acid sequence (His-Asn) of the instantly claimed SEQ ID NO: 31. See His453 and Asn454 of the chimeric polypeptide of Chong et al (fig. 1 and fig. 2). The laboratory designation BIL4_CLOTH does not distinguish the instantly claimed autoprocessing segment from that of Chong et al. The recitation of the process by which the instant autoprocessing segment is derived is a process limitation which does not structurally further limit the instantly claimed polypeptide. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP chapter 2113, Product-by-Process claims. In the instant case, the chimeric polypeptide of Chong et al comprises an autoprocessing segment comprising an amino acid sequence of SEQ ID NO: 31.

The autocleavage of the chimeric polypeptide of Chong et al results in removal of a segment of the polypeptide adjacent to an amino terminal end or carboxy terminal end of said autoprocessing segment (fig. 1) and the segment of the polypeptide adjacent to said autoprocessing segment is an amino terminal segment or carboxy terminal segment of the polypeptide (fig.1).

Chong et al teach that the segment of the polypeptide adjacent to said carboxy terminal end of said autoprocessing segment can contain an amino acid residue comprising a nucleophilic group at an amino terminal end e.g. hydroxyl group (p. 22159 column 1) or amino acid residues

such as threonine or serine (p. 22159 column 1).

Chong et al teach that autocleavage of said chimeric polypeptide results in autosplicing (fig. 1) of the segments of the polypeptide flanking said autoprocessing segment.

Chong et al teaches the concentration of dithiothreitol (25 mM or 40 mM) and pH 7.6 at which autocleavage occurs.

Chong et al teach that the chimeric polypeptide comprises an affinity tag such as maltose binding protein whose substrate is a molecule/compound is amylose (p. 22160 column 2 under purification on amylose columns).

Applicant can overcome the Chong et al rejection above my amending claim 1 to recite that the autoprocessing segment comprises *the* (instead of an) amino acid sequence set forth in SEQ ID NO: 31.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chong et al The Journal of Biological Chemistry vol. 271:22159-22168, 1996 (IDS).

Chong et al teach a chimeric polypeptide comprising an autoprocessing segment having an amino acid sequence (His-Asn) of the instantly claimed SEQ ID NO: 31. See His453 and Asn454 of the chimeric polypeptide of Chong et al (fig. 1 and fig. 2). The laboratory designation BIL4_CLOTH does not distinguish the instantly claimed autoprocessing segment from that of Chong et al. The recitation of the process by which the instant autoprocessing segment is derived is a process limitation which does not structurally further limit the instantly claimed polypeptide. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP chapter 2113, Product-by-Process claims. In the instant case, the chimeric polypeptide of Chong et al comprises an autoprocessing segment comprising an amino acid sequence of SEQ ID NO: 31.

The autocleavage of the chimeric polypeptide of Chong et al results in removal of a segment of the polypeptide adjacent to an amino terminal end or carboxy terminal end of said autoprocessing segment (fig. 1) and the segment of the polypeptide adjacent to said autoprocessing segment is an amino terminal segment or carboxy terminal segment of the

polypeptide (fig.1).

Chong et al teach that the segment of the polypeptide adjacent to said carboxy terminal end of said autoprocessing segment can contain an amino acid residue comprising a nucleophilic group at an amino terminal end e.g. hydroxyl group (p. 22159 column 1) or amino acid residues such as threonine or serine (p. 22159 column 1).

Chong et al teach that autocleavage of said chimeric polypeptide results in autosplicing (fig. 1) of the segments of the polypeptide flanking said autoprocessing segment.

Chong et al teaches the concentration of dithiothreitol (25 mM or 40 mM) and pH 7.6 at which autocleavage occurs.

Chong et al teach that the chimeric polypeptide comprises an affinity tag such as maltose binding protein whose substrate is a molecule/compound is amylose (p. 22160 column 2 under purification on amylose columns).

Chong et al does not teach the ph 7.8-8.2 and DTT concentration 0.1 mM to 20 mM at which autocleavage occurs.

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to vary the conditions e.g. pH or DTT concentration under which autocleavage of the chimeric polypeptide of Chong et al occurs to arrive at the instant pH 7.8 or 20 mM DTT respectively because Chong et al teach that autocleavage occurs at a pH 7.6 and DTT concentration 25 mM which are reasonably close to the instant pH and DTT concentration.

Claims 16 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chong et al The Journal of Biological Chemistry vol. 271:22159-22168, 1996 as applied to claims 1-12 and 14-17 in view of Jarvik et al Anu. Rev. Genet. 1998, 32:601-18.

Chong et al is set forth supra and does not teach an affinity tag wherein the substrate is a virus wherein said virus is a bacteriophage. For the purposes of this rejection, claims 16 and 18 are interpreted to mean that the affinity tag is derived from a virus/bacteriophage as it is not clear which affinity tag has a virus/bacteriophage as a substrate.

Jarvik et al teach the T7 epitope tag (p. 604 table 1, leader peptide of phage T7 and see specification p. 22 lines 31-32 to page 21 line 23) which is capable of binding a substrate such as an anti-T7 antibody (molecule/compound).

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to insert an epitope affinity tag such as a T7 tag into the chimeric polypeptide of Chong et al because Jarvik et al teach that T7 epitope tags provide a specific means to purify the tagged protein.

Claims 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chong et al The Journal of Biological Chemistry vol. 271:22159-22168, 1996 as applied to claims 1-12 and 14-17 in view of Chong et al Nucleic Acids Research, 1998 vol. 26: 5109-5115 (IDS).

Chong et al is set forth supra and does not teach an affinity tag wherein the substrate is molecule/compound such as chitin

Chong et al (1998) teach an affinity tag, CBD (chitin binding domain) inserted into a chimeric polypeptide to allow for affinity purification (p. 5109 column 2) whose substrate is chitin (see figure 1b).

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to insert an affinity tag such as CBD into the chimeric polypeptide of Chong et al (1996) because Chong et al (1998) teach that CBD allows for affinity purification of the tagged protein.

Status of the Claims

Claims 1-18 are rejected. Claims 1-6 are objected to. No claims allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Oluwatosin Ogunbiyi whose telephone number is 571-272-9939. The examiner can normally be reached on M-F 8:30 am - 5:00 pm. If attempts to reach the

examiner by telephone are unsuccessful, the examiner's Supervisory Examiner Shanon Foley can be reached on 571-272-0898.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Oluwatosin Ogunbiyi/

Examiner, Art Unit 1645

/Patricia A. Duffy/

Primary Examiner, Art Unit 1645